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Sniffing Out Emotion in Preoperative Evaluations for Epilepsy

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ABSTRACT

Surgical candidates for epilepsy need more information pertaining to possible side effects of surgical resection impacting emotional recognition of people and experiences. Specifically, for an individual what degree of lateralization is present in a brain's ability to recognize, respond to, and experience an emotion? Olfaction is processed in brain structures excised during surgery, but it overlays networks involved in other sensory modalities. Its connection to emotional memory is long established. Recognition tests of emotion evoking substances should be explored for use in Wada exams to predict the resected brain's ability to respond to stimuli for emotions such as pleasure, disgust, or affection. Whereas odor processing in the brain is largely ipsilateral to the nostril, it may further prove useful to compare a Wada evaluation to a test done simply by alternately blocking nostrils and screening for changes in perceived quality of substances. If successful, such an approach would obviate the need to involve a Wada exam.

Keywords: Emotional recognition, Olfaction, Epilepsy, Wada exam

Abbreviations: ATL: Anterior temporal lobectomy

INTRODUCTION

Anterior temporal lobectomy (ATL) is a common approach to seizure control with a proven therapeutic track record. However, as many as 7% of patients experience postoperative psychiatric disorders [1]. For a patient who experiences preoperative emotional impairment (such as can be the case following Status epilepticus), even on the scale of minutes, and comes to recognize it as such, the experience can inspire an obsessive yet warranted desire for information pertaining to the possible postoperative side effects of ATL. By impairment, it generally means a deficit of response to a stimuli such as feeling a profound indifference towards a loved one following a medical trauma [2] rather than a miss-assignment of emotion to a stimulus (a greater impairment but not one I address). In personal experience in an American hospital (the author has left mesial temporal sclerosis), preoperative assessment for vulnerability to emotional impairment is not evaluated nor is information drawn from research on others discussed with the patient (see [3] for an example of ideal procedures in France).

For a resection candidate, functional redundancy across cerebral hemispheres is valuable. Thus, a key question for decision making becomes whether or not the ability to recognize or express emotions differs between hemispheres and with much person-to-person variation. If so, is making a personal profile a source of novel and useful data for the doctor and patient to use in decision making regarding surgical resection?

Emotional recognition functions in the brain are more complex and region specific than has been previously assumed [4]. Discernment of the valence of other's response to stimuli is lateralized across hemispheres but the extent of this lateralization for different emotions varies between individuals [5]. Patients suffering from amygdala damage can have inconsistent patterns of recognition deficits [6]. Particular attention should be paid to the amygdala in preoperative assessment of risks, as it is especially important in linking affect (esp. negative affect) to stimuli from the environment or from individuals, and it has strong connections to sensory cortex [7].

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In addition to recognition of external displays of emotion (such as from music or the facial expressions of others), internal perceptions of fear, happiness and other emotions have been mapped with direct electrical stimulus to brain areas and found to originate in the amygdala with perceptions varying between the left and right hemisphere [3]. Thus the potential side effects of an ATL, both in accuracy of recognition and/or intensity of personal feeling can vary by the side of the brain operated on and from patient to patient thereby justifying a patient's desire for more information.

How then can more preoperative knowledge be gained? From the outset, let me acknowledge that no specific test can be comprehensive in any sense. I take the view that any knowledge is good and incremental gain is useful.

The Wada exam is a common part of preoperative evaluation for epilepsy surgery and could play a role in assessing a degree of emotional lateralization in an individual's brain. During its usage for localizing eloquent cortex, can it serve dual purposes? Stabell et al. [8] looked at how the Wada exam, itself, might affect emotional state. They found that the exam could trigger both euphoric and, less commonly, dysphoric changes in mood. The former occurred for one in five persons and the latter one tenth as frequently. They analyzed age, gender, amobarbital dosage, its side and sequence of its injection, and language laterality. They found no statistical differences in these variables between patients with and without emotional changes under anesthesia. Emotional responses appeared immediately and abated long before testing ended. The responses never hindered a subject's ability to follow instructions. Their results suggest that using a Wada exam in a test of emotional recognition, and even internal emotional feeling, cannot be dismissed out of hand.

In light of the effects of anesthesia on eloquent cortex (and thus communicative ability) and in light of any time concerns, a system for evaluating emotional cognition that has a quick response, high reliability, and one which may reflect trends toward other sensory systems should be useful. Something which has fast associative training capability would also be welcome. Naturally, such a system should connect closely to the hippocampus and amygdala which are removed in surgery.

Olfaction is more influential to emotional cognition [9] than other senses - the sense of smell is appetitive, i.e., central to seeking food, sexually receptive mates and other things associated to joy or pleasure. Smell also warns of dangers and triggers fear response. It is superior to other senses in cuing emotional memories far back into time [10]. Emotion may have a fundamental relationship to olfaction to a considerably greater degree than to other senses [11,12] and the two systems share extensive parts of neural networking [12].

Olfaction is processed through the hippocampus and amygdala [9]. It may also be a more potent stimulus of activity in the amygdala than are hearing and vision [13]. Olfactory and visual input stimulates activity in the hypothalamus, whereas auditory input does not [13]. Olfaction, as a trigger, is very rapid - two to three neurons lie between the olfactory epithelium and the memory and emotional structures in the brain [14]. Importantly, primary olfactory cortical functional connectivity within a hemisphere does not statistically differ between hemispheres [11].

A key concern to a method for assessing emotion in the brain is the possible influence of cultural and personal differences in relation to stimulant effects which can be quite substantial [15]. Surstromming (months old fermented fish) is perceived differently by a Scandinavian than by persons of other cultures. Age and gender related life histories also influence the emotional response to odor. A veteran is expected to have a dampened response to any negative emotional stimulus than would an adolescent. A faint smell of horse manure will simply offend some people but bring up pleasant memories of grandpa's farm to others.

A training procedure that would impart stimulus - response patterns de novo might ameliorate concerns about response variations across cultures, ages or other demographic parameters. Temporal lobe epilepsy, itself, can cause deficits in olfactory perception of pleasantness, familiarity and other parameters [16]. Training de novo might address this problem. Emotional associations to odors are not innate, but rather, learned and new associations with novel odors can be trained *in situ* and remain stable for a week if not longer [15].

One example of what training can entail is the work of Herz et al. [17] who manipulated research participants' associations to odor using culturally relevant entertaining and funny films of 15 min in duration. They also used gambling games that were secretly biased in favor of the subject. All the while, the individual was selectively exposed to ambient odors to be used as emotional stimulants in later research.

Emotional connections to odors already have a broad study base [18,19]. In addition to established test methodologies, an extensive amount of research results exists for a broad catalog of odors and feelings linked to them [10,18,20,21] (see appendices A and B in [15] for detailed examples used in verbal assessments). Hence, experiments in clinical usage do not need to break new ground in materials used.

Given that the Wada test attempts to impair language, responses to stimulated feelings (or the lack thereof) need to be conveyed non-verbally. Research methods involving an assessment of affect have also used non-verbal methodologies. An affect grid allows an individual to rate pleasantness and arousal from a stimulus simply by placing a

mark on a grid. The technique is reviewed extensively by Toet et al. [22] who further describe an approach for testing children that uses emojis (the cartoon faces employed in such web sites as Facebook to convey sentiment). No language is involved, ameliorating at least some concern regarding the left side bias of language. Of course heart rate and skin conductance have long been used to such ends. Skin conductance correlates to emotional arousal, though heart rate may be less predictable [18].

As a side note, a visionary yet feasible approach to training the olfactory system outside of a clinical setting hypothetically requires only essential oils, disposable masks to conduct odors, a room fan (for purging the environment) and an internet connection. Movie clips or games can readily be tailored to stimulate to any set of emotions, be viewed via the internet, and procedure adherence recorded remotely. Likewise, olfactory cues can be self-administered with the use of blindly labeled vials with a single use disposable mask (blind methodologies are critical [20]). Intervals between training for different stimulants can be indicated remotely with or without close human supervision. In-home olfactory training also has a familiar and relaxed environment. Remote patient monitoring of a simpler nature is already used pre- and post-operatively in cardiac surgery and also pace-maker monitoring (personal experience) [22].

While my thoughts generally assume the administration of a Wada exam, one exciting characteristic of the olfactory system is that smells are primarily processed ipsilaterally to the individual receiving nostril with much reduced contralateral processing, though this pattern is by no means absolute [23]. Sensory cells project exclusively to the ipsilateral olfactory bulb which connects exclusively to the ipsilateral olfactory cortex [24]. The ramifications for anesthesiology are that it might be possible to forgo it in favor of a simple nostril plug. EEG results provide useful information and have a huge study base to draw upon [19]. In the time interval between ipsilateral and contralateral responses to stimulation, an EEG might provide pertinent information regarding response locations and intensities thereby providing some information about the response regions of the brain for a stimulus without needing to anesthetize half of the brain and coping with artificially induced euphoria/dysphoria. Nevertheless, the issue of predominant ipsilateral processing is not completely resolved and any optimism for such an approach must remain guarded [25].

CONCLUSION

There are deeper concerns to temporal lobe resection than just the preservation of eloquent cortex. Preserving a full range of emotional faculties can be a patient's main concern. Sensory systems that offer direct insight into how we associate emotions to our physical and social environment under artificial brain impairment are valuable to judging the impact of ATL on such faculties. Associations include recognizing expressions in or from others via sensory cues, feeling emotions stimulated within us and combinations of each. Of further value is a sensory system that surrogates other senses to a great extent. The olfactory system is such a system and relevant psychological background research is quite substantial thus facilitating rapid optimization of methodologies, e.g. choosing odors to use or defining time intervals of interest on EEG results. Olfactory responses to stimuli can readily be trained - calibrated - to preclude cultural and other artifacts between people from distorting results. As such, it warrants deeper attention for a role in preoperative patient evaluation for ATL.

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